



Distinguishing Ischemic Cardiomyopathy From Nonischemic Dilated Cardiomyopathy With Coronary Echocardiography

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Trans thoracic echocardiographic examination of the proximal left coronary system was performed in 59 patients who had dilated cardiomyopathy to determine if this technique could distinguish between ischemic and nonischemic dilated cardiomyopathy. With use of annular array transducers (3.5 or 5 MHz) and digital image processing, echocardiographic visualization of the coronary arteries was successful in 55 (93%) of 59 patients. As assessed by coronary angiography, 32 subjects had ischemic cardiomyopathy and 27 had nonischemic cardiomyopathy.

Twenty-seven (84%) of the 32 patients who had coronary artery disease and 24 (89%) of the 27 patients with nonischemic cardiomyopathy were correctly identified. The accuracy of coronary echocardiography was 86% in the entire study group and 93% when patients with inadequate studies were excluded. All

subjects who had ischemic cardiomyopathy had evidence of disease by coronary echocardiography or segmental wall motion abnormalities. Multivariate analysis permitted correct classification of 93% of all subjects based on the results of the coronary echocardiogram, evaluation of segmental wall motion and a history of prior myocardial infarction. The correct diagnosis was made in 86% when the results of coronary echocardiography were excluded from analysis using all other echocardiographic and clinical variables.

Trans thoracic coronary echocardiography can be performed with a high degree of success in patients with dilated ventricles and the technique can reliably distinguish between ischemic and nonischemic dilated cardiomyopathy.

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Various noninvasive methods have been employed for the purpose of distinguishing dilated cardiomyopathy due to coronary artery disease (ischemic cardiomyopathy) from nonischemic dilated cardiomyopathy (1-11). The correct diagnosis may not be apparent from the history, physical examination, electrocardiogram (ECG) or assessment of regional systolic function (1-3,12,13). The coronary arteries in idiopathic dilated cardiomyopathy are frequently enlarged and free of obstruction (1). In contrast, severe multivessel disease is the most frequent finding in patients who have cardiomyopathy due to coronary artery disease (14).

Direct visualization of the coronary arteries by trans thoracic two-dimensional echocardiography may be the ideal noninvasive method for distinguishing the cardiomyopathies. This technique has been the subject of investigation for more than a decade (15-20). Until recently, application of

the technique has been confined to detection of left main coronary artery disease because only limited portions of the proximal left coronary system could be visualized (16,17,20). The development of high frequency annular phased array transducers and computers that digitize echocardiographic frames in real time have enabled visualization of greater portions of the proximal left coronary artery system (21-23). Additionally, left ventricular dilation also permits visualization of greater portions of coronary vessels that are oriented in two-dimensional planes parallel to the length of the vessel. The purpose of this study was to determine both the feasibility and the accuracy of trans thoracic coronary echocardiography for distinguishing ischemic and nonischemic dilated cardiomyopathy.

Methods

Study patients. The initial study group consisted of 16 patients with dilated cardiomyopathy and known coronary anatomy who underwent coronary echocardiography to determine the feasibility of this imaging technique. The remaining subjects were selected from all patients who were referred to the Indiana University Echocardiography Laboratory during a 3-year period for evaluation of left ventricular systolic function. Inclusion criteria were 1) increased left ventricular end-diastolic diameter >5.2 cm; 2) reduced left

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ventricular systolic function characterized by a fractional shortening <0.18 or a fractional area change <0.36 (24). Subjects who were prospectively evaluated underwent coronary angiography within 3 months of echocardiography. Patients were excluded if they had a history and echocardiographic evidence of significant valvular heart disease or long-standing hypertension with echocardiographic evidence of left ventricular hypertrophy (mid-anterior septum and mid-posterior wall thickness >1.2 cm in diastole). Patients too ill to be transported to the echocardiography laboratory were also excluded. A consecutive series of patients was not enrolled because of the exclusion criteria and the requirement for coronary angiography. Patients were not selected on the basis of the quality of echocardiographic images.

Echocardiography. Two-dimensional echocardiograms were performed with commercially available equipment (Ultramark-8, Advanced Technology Laboratories) to evaluate global and regional left ventricular systolic function and chamber size. Routine two-dimensional scans were performed with a 3.5-MHz annular phased array transducer or a 3-MHz mechanical sector scanner that was also employed for pulsed wave Doppler examinations.

Coronary echocardiograms were obtained with a 3.5-MHz or a 5-MHz annular phased array transducer. The left main coronary artery and the most proximal portion of the left anterior descending artery were visualized in the short-axis plane by previously described methods (22). Coronary artery images were digitized on-line by a manually triggered mechanism that captured 32 consecutive fields at 33-ms intervals. The resulting sequence of images consisted of multiple tomographic "slices" of the coronary arteries acquired as they passed in and out of the imaging plane. The sequence of images was arranged in a quad screen format that permitted simultaneous display of four separate sets of images. The transducer plane was slightly altered during acquisition of each set of images to enhance visualization of the proximal left circumflex artery and left anterior descending artery as both structures turn out of the imaging plane used to visualize the left main coronary artery. Additional sets of images were obtained with an apical five-chamber view if adequate visualization could not be achieved in the short-axis plane (17). The completed study was permanently stored on 5.25-in. (13.34-cm) floppy disks for analysis.

Echocardiogram analysis. The fractional shortening and fractional area change were determined in each subject from two-dimensional echocardiographic measurements (25). Segmental wall motion was qualitatively assessed by a single observer who knew the subject's clinical history but not the results of coronary echocardiography and angiography. In addition, the left ventricle was assessed for the presence of myocardial scar and aneurysm. Myocardial scar was defined as an akinetic region with absent systolic thickening and less diastolic thickness than that of regions with normal wall motion. Left ventricular aneurysm was defined as a multi-segment region exhibiting reduced diastolic thickness and dilation in both diastole and systole.

Coronary echocardiograms were interpreted by two observers who had no knowledge of the clinical history or results of two-dimensional echocardiography and coronary angiography. The analysis system permitted replay of a portion or a complete image sequence as a continuous loop or frame by frame analysis. The system also allowed gray scale manipulation to optimize detection of high intensity echoes that were interpreted as evidence of coronary artery disease (19). Studies were considered adequate for interpretation if the left main coronary artery could be visualized together with any portion of the left anterior descending or left circumflex artery beyond the bifurcation.

The criteria used to diagnose ischemic cardiomyopathy were 1) globular high intensity echoes that occupied $\geq 50\%$ of the lumen diameter of the left main, proximal left anterior descending or circumflex artery in any one frame; or 2) presence of intraluminal high intensity echoes on three consecutive frames or for 50% of all the frames in which the artery was visualized. Nonischemic cardiomyopathy was diagnosed if high intensity echoes were absent or if intraluminal high intensity echoes were present without lumen encroachment. A third observer reviewed the studies in blinded manner in cases of disagreement between the first two observers.

Coronary angiography. All patients underwent coronary angiography, which was performed and interpreted by a cardiologist who had no knowledge of the coronary echocardiographic results. Subjects who had $\geq 50\%$ reduction in lumen diameter of a major epicardial coronary artery were defined as having significant coronary artery disease and ischemic cardiomyopathy. Subjects who had $<50\%$ angiographic narrowing of lumen diameter were defined as having nonischemic dilated cardiomyopathy.

Statistical analysis. Clinical and echocardiographic variables were compared between those with ischemic and nonischemic dilated cardiomyopathy by using the Fisher exact test for variables with two categories. The chi-square contingency table test was used for variables with more than two categories and continuous variables were analyzed with unpaired *t* tests. Discriminant analysis was performed to identify the combination of variables that most accurately classified the two groups of subjects.

Results

Coronary angiography. By coronary angiographic criteria, 32 patients had ischemic cardiomyopathy and 27 had nonischemic dilated cardiomyopathy. Of the patients with ischemic cardiomyopathy, 5 had single-vessel, 13 had double-vessel and 11 had triple-vessel disease; 3 patients had significant disease of the left main coronary artery. Coronary artery disease involved the left anterior descending artery in 29 patients, the left circumflex artery in 21 and the right coronary artery in 22. Twenty-seven patients (84%) had angiographically significant disease judged to be within the first third of the left anterior descending or left circumflex

Table 1. Ischemic Cardiomyopathy and Nonischemic Dilated Cardiomyopathy: Clinical and Echocardiographic Variables in 59 Patients

	Ischemic Cardiomyopathy (n = 32)	Nonischemic Cardiomyopathy (n = 27)	p Value
Age (years)	56 ± 11	47 ± 15	0.015*
Male gender (no.)	29 (91%)	22 (81%)	0.450
Preceding viral illness (no.)	0 (0%)	7 (26%)	0.003*
Cardiac risk factors (no.)	30 (94%)	15 (56%)	<0.001*
History of MI (no.)	16 (50%)	1 (4%)	<0.001*
Angina (no.)	14 (44%)	6 (22%)	0.103
Q waves on ECG (no.)	19 (59%)	2 (7.5%)	<0.001*
LVDd (cm)	6.01 ± 0.68	6.47 ± 0.75	0.018*
Fractional shortening	0.14 ± 0.06	0.12 ± 0.06	0.216
Proximal aortic change	0.24 ± 0.11	0.22 ± 0.09	0.367
Segmental WMA	26 (81%)	6 (22%)	<0.001*
Scar	11 (34%)	0 (0%)	<0.001*
Aneurysm	4 (13%)	0 (0%)	0.118
Normal baseline septal motion	8 (25%)	1 (4%)	0.031*

*Statistically significant difference between groups. Values with a ± indicate mean values ± SD. ECG = electrocardiogram; LVDd = left ventricular diastolic dimension; MI = myocardial infarction; WMA = wall motion abnormality.

artery. A single patient had significant disease involving only the right coronary artery; in this patient the left anterior descending artery had <50% reduction in lumen diameter.

The coronary angiographic findings were normal in 23 patients with nonischemic cardiomyopathy. Three other patients had mild lumen irregularities and one patient had 40% stenosis of a diagonal branch.

Clinical and left ventricular echocardiographic data (Table 1). Subjects with ischemic cardiomyopathy were older and more frequently had a history of prior myocardial infarction, ECG Q waves and one or more risk factors than did those with nonischemic cardiomyopathy. Patients with ischemic cardiomyopathy were also more likely to have segmental wall motion abnormalities, scar and normal wall motion of the basal anterior septum. The clinical and ventricular echocardiographic predictors of ischemic cardiomyopathy had low sensitivity with the exception of risk factors (94%) and abnormal segmental wall motion (81%). Subjects with nonischemic cardiomyopathy were more likely to have a history suggestive of antecedent viral illness and a larger mean diastolic dimension. Left ventricular systolic function was comparable in the groups with and without ischemic cardiomyopathy.

Coronary echocardiography. The proximal left coronary system was adequately visualized in 55 (93%) of the 59 patients. Three patients with ischemic cardiomyopathy and one patient with nonischemic cardiomyopathy had inadequate studies. Among the studies considered adequate for

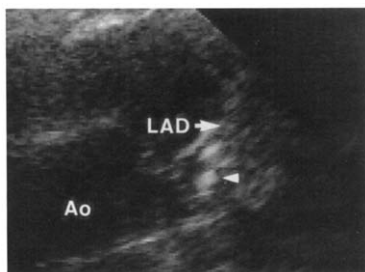


Figure 1. Coronary echocardiogram in a subject with ischemic cardiomyopathy demonstrating high intensity echoes narrowing the origin of the left anterior descending coronary artery (LAD) and obstructing the origin of the left circumflex coronary artery (arrowhead). Coronary angiography showed calcification of the left main coronary artery, severe stenosis of the left anterior descending coronary artery and occlusion of the circumflex artery. Ao = aorta.

interpretation, there was disagreement between the first two observers in eight studies; four of these studies were of reduced quality. The proximal left anterior descending artery was visualized in 55 patients (93%) and the left circumflex artery in 34 (58%). When inadequate studies were included in the analysis, the sensitivity of coronary echocardiography was 84% (27 of 32) and the specificity was 89% (24 of 27) for detection of ischemic cardiomyopathy. When inadequate studies were excluded, the sensitivity and specificity of coronary echocardiography for detection of ischemic cardiomyopathy were 93% (27 of 29) and 92% (24 of 26), respectively. The diagnostic accuracy was 93% (51 of 55).

Ten patients with ischemic cardiomyopathy had no history of myocardial infarction or ECG Q waves and three patients with nonischemic cardiomyopathy had either Q waves or a history of infarction. The accuracy of coronary echocardiography was 85% (11 of 13) in this subgroup of patients who were incorrectly classified by these clinical variables.

Patients who had ischemic cardiomyopathy tended to have multiple high intensity echoes in the proximal left coronary arteries (Fig. 1); less commonly, isolated, discrete high intensity echoes were found (Fig. 2). These intraluminal echoes were absent in patients who had nonischemic cardiomyopathy (Fig. 3). The arteries tended to be large and easily visible in these patients.

All patients with ischemic cardiomyopathy could be identified by coronary echocardiographic abnormalities or by the presence of abnormal segmental wall motion. Both coronary echocardiographic abnormalities and abnormal segmental wall motion were absent in 67% of patients with nonischemic cardiomyopathy.

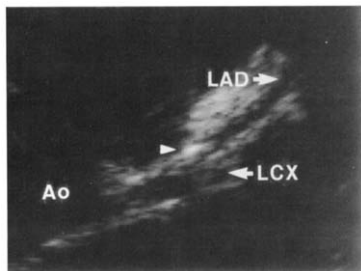


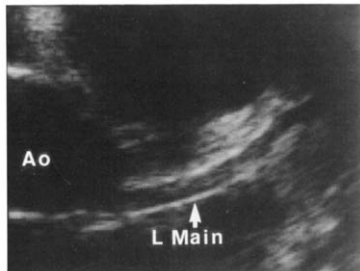
Figure 2. Coronary ultrasound demonstrating a discrete high intensity echo (arrowhead) obstructing the origin of the left anterior descending coronary artery (LAD) which was confirmed by angiography. LCX = left circumflex coronary artery; other abbreviation as in Figure 1.

Multivariate analysis permitted correct identification of 93% of all subjects on the basis of results of coronary echocardiography, analysis of segmental wall motion and history of myocardial infarction. When the results of coronary echocardiography were excluded from this analysis, 83% of subjects were correctly identified. When coronary echocardiography was excluded from a discriminant analysis that included all other variables, 86% of subjects were correctly classified.

Discussion

Diagnostic utility of noninvasive methods. Various imaging modalities have been investigated in an effort to find an

Figure 3. Large, unobstructed left main coronary artery (L main) and proximal left anterior descending coronary artery in a patient with nonischemic cardiomyopathy. The origin of the left circumflex coronary artery is not seen in this frame. Other abbreviation as in Figure 1.



accurate and cost-effective noninvasive method for distinguishing cardiomyopathy due to ischemic heart disease from nonischemic dilated cardiomyopathy. The differential diagnosis may still be in doubt after evaluation of the history and ECG, particularly in middle-aged men with some coronary risk factors (2,12,13,26). Both cardiac fluoroscopy and thallium scintigraphy have been employed as methods for distinguishing between these cardiomyopathies (4-9). Positron emission tomography has been advocated as a potentially more accurate method for differentiating the two groups by providing information on both perfusion and metabolism (10). Detection of segmental wall motion abnormalities by nuclear angiography or echocardiography does not accurately identify patients who have ischemic cardiomyopathy (3,11). Segmental abnormalities are not confined to patients with coronary artery disease and these abnormalities may be absent in those with advanced coronary disease and marked left ventricular dilation (11).

Two-dimensional echocardiography could enhance the specificity of regional abnormalities for ischemic cardiomyopathy by identifying patients who have an aneurysm or thinned, akinetic segments suggesting myocardial scar. Left ventricular aneurysm and scar formation, found on gross inspection of the myocardium, occur in <15% of subjects with nonischemic dilated cardiomyopathy (27). In this study, aneurysm and scar were absent in such subjects. However, aneurysm and scar were insensitive indicators of significant coronary artery disease.

Technique and diagnostic utility of coronary echocardiography. The proximal left coronary artery was visualized in 93% of subjects. Previous transthoracic echocardiographic studies (16,17,21,22) have reported lower rates of success for imaging of the left coronary artery. The success of coronary echocardiography in our study group was enhanced by the increased left ventricular size, which reduced the angles of curvature of the coronary arteries and permitted imaging of longer portions in any one plane. Coronary visualization was more difficult in subjects who had ischemic cardiomyopathy because of the smaller left ventricular size and higher frequency of obstructive lung disease. The smaller left ventricular size increases the angle of curvature, making visualization more difficult. In addition, obstructive lung disease decreases the ability to visualize some cardiac structures.

The interobserver variability for determination of significant disease was not unexpected. This variability may be due in part to the investigators' attempts to interpret studies that were of suboptimal quality. Previous studies (19,22) have shown that the distinction between diseased and normal arteries can be based on the presence or absence of high intensity echoes. However, the echocardiographic criteria for determining the severity of coronary artery disease that correlate best with the results of coronary angiography have not been established. The criteria employed in this study accurately identified patients with cardiomyopathy when subjects with inadequate echocardiograms were excluded.

The high accuracy of coronary echocardiography in this study may be explained both by patient selection and by the diffuse nature of coronary artery disease in the subjects with ischemic cardiomyopathy. Those who had cardiomyopathy due to long-standing hypertension were excluded from this study. A higher frequency of mild, nonobstructive coronary artery disease might be expected in such patients than in patients with nonischemic or idiopathic dilated cardiomyopathy. The echocardiographic differentiation of patients with cardiomyopathy who have mild coronary disease (primarily intraluminal high intensity echoes) from those who have obstructive coronary artery disease (intraluminal and intraluminal echoes) may be more difficult than the differentiation of patients with virtually no disease from those with obstruction. Also excluded from this study were patients who had significant valvular heart disease, in whom aortic and mitral valve thickening and calcification may mimic high intensity coronary artery echoes.

Pathologic studies in patients with prior myocardial infarction have demonstrated evidence of scattered or diffuse atherosclerotic disease involving multiple arterial segments. Dash et al. (28) in an angiographic study demonstrated that patients with coronary artery disease and congestive heart failure had a higher "coronary jeopardy score" reflecting more extensive and proximally located disease than that of patients without heart failure. In patients who have multivessel disease including the left anterior descending artery, the correlation is closer between measurements of coronary flow and lumen area than between flow and percent diameter stenosis because of diffuse arterial narrowing (29). Coronary artery echocardiography enables detection of coronary disease in arterial segments that have little or no angiographic evidence of disease (30). The proximal and diffuse nature of disease in ischemic cardiomyopathy explains the high sensitivity of transthoracic coronary echocardiography, in which visualization of the coronary artery may be proximal to the portion demonstrating the greater angiographic disease.

In the diagnostic evaluation of dilated cardiomyopathy, the critical task is detection of all patients who have significant coronary artery disease. Apart from vasodilator therapy, little can be done to alter the natural history of idiopathic dilated cardiomyopathy (31). The treatment options for ischemic cardiomyopathy are broader and may lead to prolonged survival and improvement of left ventricular function. In this study, all patients who had significant coronary artery disease were identified by coronary echocardiography or by the presence of segmental wall motion abnormalities.

Study limitations and clinical application of coronary echocardiography. Successful coronary visualization was not universally achieved, and the accuracy of coronary echocardiography was only 86% when all patients were included in the analysis. The results obtained in this study using digital image storage and high frequency annular array transducers may not be directly applicable to laboratories employing other techniques for transthoracic coronary echocardiography.

No attempt was made to image the right coronary artery. Patients whose left ventricular dysfunction is primarily due to disease of the right coronary artery may be misidentified by examination of only the left coronary system. However, limitation of the examination to the left coronary artery may not significantly reduce the sensitivity for ischemic cardiomyopathy. Of 66 patients who had ischemic cardiomyopathy, Yatteau et al. (14) found none with isolated right coronary artery involvement.

The utility of two-dimensional transthoracic echocardiography for examination of the coronary arteries was recently reported by Reichert et al. (32), who successfully visualized the left main and proximal left anterior descending and left circumflex arteries in 88%, 52% and 88% of patients, respectively. Significant coronary stenoses were correctly identified in the majority of patients who had disease of the left main or left anterior descending artery but not in those with left circumflex disease. In the hands of these investigators (32), Doppler color flow mapping showed promise as a method for detection of coronary stenoses by identifying sites of disturbed flow signals. Iliceto et al. (33) recently demonstrated that coronary flow reserve in normal and diseased left anterior descending arteries could be estimated by transthoracic pulsed wave Doppler examination during dipyridamol infusion. These alternative methods for examining the coronary arteries were not available when the current cardiomyopathy study was initiated in this laboratory.

Differentiation of ischemic cardiomyopathy from nonischemic dilated cardiomyopathy solely on the basis of angiographic criteria is not entirely precise. Cardiomyopathy of unknown cause may coexist with coronary artery disease that may not be the cause of ventricular dysfunction (34).

Conclusions. Transthoracic two-dimensional echocardiography of the proximal left coronary artery was performed with a high degree of success in patients who had a dilated left ventricle. In patients who had adequate studies, coronary echocardiography accurately distinguished ischemic cardiomyopathy from nonischemic cardiomyopathy. Multivariate analysis permitted accurate differentiation of the two conditions in the entire study group. Maximal sensitivity for detection of ischemic cardiomyopathy was achieved by combining the results of coronary ultrasound and analysis of regional wall motion.

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